

HPV16/18 Type 3 transformation zone

Systematic review report

PICO

This systematic review addresses the following PICO which is summarised in detailed in Table 1.

For women who have a HPV16/18 positive test, no referral cytology or negative, pLSIL or LSIL cytology and a type 3 transformation zone (unsatisfactory colposcopy) what is the safety and effectiveness of a random or non-targeted biopsy, endocervical brush/lavage, endocervical curettage or endometrial sampling at colposcopy in detecting CIN3+ and reducing cervical cancer incidence and mortality?

Table 1. PICO components

Population	Study design	Intervention	Control	Outcomes
Women who have a HPV16/18 positive test and type 3 transformation zone (unsatisfactory colposcopy) and 1. no referral cytology 2. negative, pLSIL or LSIL cytology	Screening randomized or Pseudo-randomized controlled trial	Additional procedures (random or non-targeted biopsy, or endocervical brush/lavage, endocervical curettage or endometrial sampling) at colposcopy and confirmatory cytology to guide management	No additional procedures at colposcopy Confirmatory cytology only to guide management	Cervical cancer mortality Cervical cancer Diagnosis

HPV = human papillomavirus; LSIL = low-grade squamous intraepithelial lesion; pLSIL = possible LSIL

1. METHODS

1.1 Selection Criteria

Table 2. Selection criteria

	Inclusion criteria	Exclusion criteria
Study type	Intervention	
Study design	Screening randomized or pseudorandomized controlled trial	Cohort studies Case-control studies
Population	Women who have a HPV16/18 positive test and no referral cytology or negative, pLSIL or LSIL cytology and a type 3 transformation zone (unsatisfactory colposcopy)	
Intervention	Additional procedures <ul style="list-style-type: none"> • random or non-targeted biopsy, • endocervical brush/lavage • endocervical curettage • endometrial sampling at colposcopy and confirmatory cytology to guide management	
Comparator	Confirmatory cytology only to guide management	
Outcome	Cervical cancer mortality Cervical cancer diagnosis	
Publication date	2005 onwards	
Publication type	Peer-reviewed journal article or letter or comment that reports original data	Conference abstract Editorial Letter or article that does not report original data
Language	English	

HPV = human papillomavirus; LSIL = low-grade squamous intraepithelial lesion; pLSIL = possible LSIL

1.2 Definitions and terminology

For the purposes of this review:

Cervical cancer refers to primary cervical cancer

Transformation zone is the region of the cervix where the columnar epithelium has been replaced and/or is being replaced by the new metaplastic squamous epithelium

Type 3 transformation zone (previously 'unsatisfactory colposcopy') is when part or the entire upper limit of the transformation zone cannot be seen in the cervical canal

Unsatisfactory colposcopy is a colposcopy in which the transformation zone is not fully visible (Jordon 2008).

1.3 Guidelines

Relevant recent (2015 onwards) guidelines were identified by scanning the citations identified by the literature search (described in section 1.4 below) and by searches of the following websites and databases in February and March:

- International Health Technology Assessment (HTA) database
- Guidelines International Network (GIN) database
- National Institute for Health and Care Excellence (NICE) Guidelines website
- Scottish Intercollegiate Guidelines Network (SIGN) website
- NHS England website
- Public Health Wales website
- World Health Organisation website
- The American Cancer Society website
- The American college of Obstetricians and Gynecologists website
- U.S. Preventive Services Task Force website
- University of Michigan Rogel Cancer Centre website
- The American Society of Clinical Oncology website
- NCCN Clinical Practice Guidelines in Oncology website
- British Columbia Medical Association website
- Health Canada
 - Canadian Task Force on Preventive Health Care (CTFPHC) Guidelines (2016) website
- Toward Optimized Practice (TOP Alberta doctors) website
- Cancer Care Ontario website
- European Society of Medical Oncologists (ESMO) website
- The Danish Health and Medicines Authority website
- Haute Autorite de Sante website

To be considered for adoption by the Working Party, guidelines had to be evidence-based and meet the pre-specified criteria of scores of greater or equal to 70% for the following domains: rigour of development, clarity of presentation and editorial independence of the AGREE II instrument (<http://www.agreetrust.org/resource-centre/agree-ii/>). Guidelines were not considered for adoption if they were not based on systematic reviews of the evidence i.e. did not report using systematic

methods to search for evidence, did not clearly describe the criteria for selecting the evidence or did not assess the risk of bias or where this is not possible, appraise the quality of the evidence.

1.4 Literature searches

Medline (including MEDLINE Epub Ahead of Print, I-Process & Other Non-Indexed Citations), Embase and CENTRAL databases were searched on 13th March 2023 combining text terms and database-specific subject headings for HPV, cervical cytology, transformation zone, colposcopy and randomised controlled trials. Searches were limited to articles published in English from 1st January 2005 onwards and were designed to identify potentially relevant trials in populations that included Aboriginal and Torres Strait Islander peoples. A complete list of the terms used is included as Appendix A. On 3rd March 2023 the Cochrane Database of Systematic Reviews was searched from inception using the search terms “human papilloma virus” and “colposcopy” and the INAHTA database was searched from 2005 onwards using the search terms “colposcopy”, “HPV” and “human papilloma virus”. Reference lists of included articles, recent relevant guidelines and systematic reviews were checked for potential additional articles.

1.5 Risk of bias assessments

For included studies risk of bias assessments using the Cochrane Collaboration Risk of Bias-II tool (Sterne 2019) were planned.

1.6 GRADE assessment of the certainty of the evidence

GRADE assessments were planned to assess the certainty of the body of evidence for each outcome. (<https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence>).

1. RESULTS

2.1 Guidelines searches

Twenty-nine potentially relevant guidelines were identified. At least some recommendations in six of these were based on systematic reviews published in English. Of these, none included recommendations that addressed the question of interest (Appendix B).

2.2 Literature searches

Figure 1 outlines the process of identifying relevant articles for this systematic review update. The combined Medline, Embase and CENTRAL search identified 130 unique citations and the search of the Cochrane Database of Systematic Reviews and INAHTA database identified 140 citations, resulting in total of 270 citations. Titles and abstracts were examined by one reviewer; no articles were retrieved for a more detailed evaluation.

No randomised controlled trials were found that met the inclusion criteria. No trials that included Aboriginal or Torres Strait Islander peoples were identified.

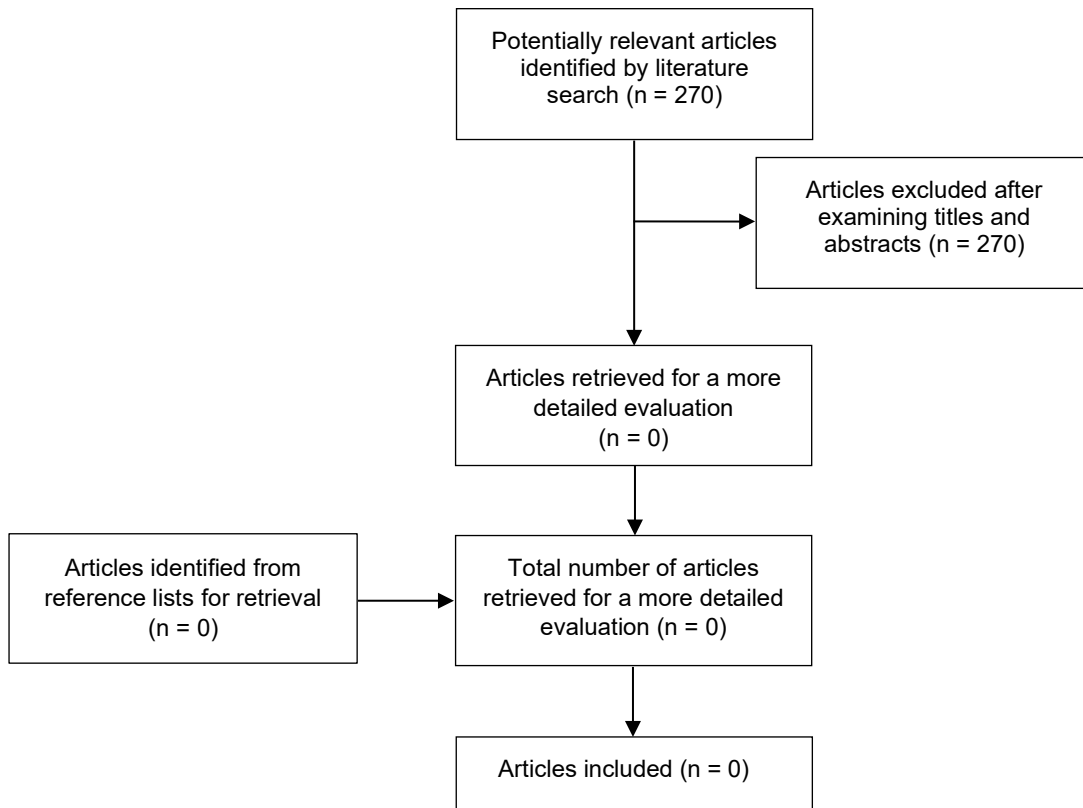


Figure 1. Process of inclusion and exclusion of studies for the systematic review update.

REFERENCES

Jordan J, Arbyn M, Martin-Hirsch P, et al. European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, part 1. *Cytopathology*. 2008;19(6):342-354.

Sterne JA, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; 366: I4898.

APPENDICES

Appendix A: Medline, Embase and CENTRAL database (via Ovid platform) search strategy

Database(s): **Embase Classic+Embase** 1947 to 2023 March 10, **Ovid MEDLINE(R) ALL** 1946 to March 10, 2023, **EBM Reviews - Cochrane Central Register of Controlled Trials** February 2023

Search Strategy:

#	Searches
1	HPV.tw.
2	hr\$HPV.tw.
3	papillomavirus.tw.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	exp Vaginal Smears/
9	((cervi* or vagina* or pap) and (smear* or screen* or test*)).tw.
10	papanicolaou.tw.
11	LBC.tw.
12	cytolog\$.tw.
13	cervical dysplasia.tw.
14	(cervi* adj5 dysplasia).tw.
15	(dyskaryosis or dyskariosis).tw.
16	ASCUS.tw.
17	ASC US.tw.
18	ASC\$US.tw.
19	ASC R.tw.
20	(atypical squamous adj4 cervi\$.tw.
21	atypical endocervical.tw.
22	atypical gland\$.tw.
23	AGUS.tw.
24	((borderline or low-grade) adj3 abnormal\$.tw.
25	((borderline or low-grade) adj3 cytology).tw.
26	SIL.tw.
27	LSIL.tw.
28	L-SIL.tw.
29	LGSIL\$.tw.
30	pLSIL\$.tw.
31	dLSIL\$.tw.
32	low grade squamous \$epithelial lesion\$.tw.
33	low-grade squamous \$epithelial lesion\$.tw.
34	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35	exp Colposcopy/
36	colposcop\$.tw.
37	35 or 36
38	squamocolumnar junction.tw.
39	SCJ.tw.
40	TZ.tw.
41	Type 3.tw.
42	Transformation zone.tw.
43	(T zone or t-zone).tw.

#	Searches
44	(colposcop* adj5 (unsatisfactory or satisfactory or adequate or normal or negative)).tw.
45	38 or 39 or 40 or 41 or 42 or 43 or 44
46	randomized controlled trial.pt.
47	controlled clinical trial.pt.
48	placebo.ab.
49	randomi?ed.ab.
50	randomly.ab.
51	trial.ab.
52	groups.ab.
53	46 or 47 or 48 or 49 or 50 or 51 or 52
54	exp animals/ not humans.sh.
55	53 not 54
56	7 and 34 and 37 and 45 and 55
57	limit 56 to english language
58	limit 57 to yr="2005 -Current"
59	remove duplicates from 58

Used the Cochrane sensitivity maximizing filter for identifying randomized controlled trials in Medline (<https://training.cochrane.org/handbook/current/chapter-04-technical-supplement-searching-and-selecting-studies> accessed 8/03/2023).

Appendix B: Potentially Relevant Guidelines reportedly based on systematic reviews

Developer	Publication or link	Title	Year	Reasons for not adopting
U.S. Preventive Services Task Force	https://jamanetwork.com/journals/jama/fullarticle/2697704 https://www.ncbi.nlm.nih.gov/books/NBK526306/	Screening for cervical cancer	2018	No relevant recommendations
WHO	https://www.who.int/publications/i/item/9789240030824	WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition	2021	No relevant recommendations
WHO	Santesso N, Mustafa RA, Schunemann HJ et al. (2016) Int J Gynaecol Obstet: 132(3):252-8	World Health Organization Guidelines for treatment of cervical intraepithelial neoplasia 2-3 and screen-and-treat strategies to prevent cervical cancer	2016	No relevant recommendations
NICE	https://www.nice.org.uk/guidance/dg32	Adjunctive colposcopy technologies for assessing suspected cervical abnormalities	2018	No relevant recommendations
Saudi Arabia Ministry of Health	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6074318/	Clinical Practice Guidelines on the Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention in Saudi Arabia	2016	No relevant recommendations
Italian Group on Cervical Screening	https://www.imrpress.com/journal/EJGO/42/5/10.31083/j.ejgo4205157	Evidence-based guidelines for follow up of women treated for cervical intraepithelial neoplasia grade 2 or 3 (CIN2/3) in Italian screening programmes	2021	No relevant recommendations